

Social recovery therapy in combination with early intervention services for enhancement of social recovery in patients with first-episode psychosis (SUPEREDEN3): a single-blind, randomised controlled trial

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SUMMARY

Background: Provision of early intervention services has increased the rate of social recovery in patients with first episode psychosis; however, many individuals have continuing severe and persistent problems with social functioning. We aimed to assess the efficacy of early intervention services augmented with social recovery therapy in patients with first-episode psychosis. The primary hypothesis was that social recovery therapy plus early intervention services would lead to improvements in social recovery.

Methods: We did this single-blind, phase 2, randomised controlled trial (SUPEREDEN3) at four specialist early intervention services in the UK. We included participants who were aged 16–35 years, had non-affective psychosis, had been clients of early intervention services for 12–30 months, and had persistent and severe social disability, defined as engagement in less than 30 h per week of structured activity. Participants were randomly assigned (1:1), via computer-generated randomisation with permuted blocks (sizes of four to six), to receive social recovery therapy plus early intervention services or early intervention services alone. Randomisation was stratified by sex and recruitment centre (Norfolk, Birmingham, Lancashire, and Sussex). By necessity, participants were not masked to group allocation, but allocation was concealed from outcome assessors. The primary outcome was time spent in structured activity at 9 months, as measured by the Time Use Survey. Analysis was by intention to treat.

Findings: Between Oct 1, 2012, and June 20, 2014, we randomly assigned 155 participants to receive social recovery therapy plus early intervention services (n=76) or early intervention services alone (n=79); the intention-to-treat population comprised 154 patients. At 9 months, 143 (93%) participants had data for the primary outcome. Social recovery therapy plus early intervention services was associated with an increase in structured activity of 8.1 h (95% CI 2.5–13.6; $p=0.0050$) compared with early intervention services alone. No adverse events were deemed attributable to study therapy.

Interpretation: The findings show a clinically important benefit of enhanced social recovery for the SRT plus EIS group on the primary outcome of structured activity.

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BACKGROUND

The provision of Early Intervention Services (EIS) for first episode psychosis (FEP) has resulted in considerable gains in social outcome in comparison to traditional more generic mental health services for this group¹⁻³. Estimates of the rate of social recovery outcomes before the provision of EIS were as low as 15% making either a partial or full social recovery at two years⁴. EIS provide a range of interventions that aim to facilitate social recovery, including recovery oriented intensive outreach case management^{5,6}. The provision of EIS has improved the rate of social recovery to between 40% and 60%^{4,7}.

Nevertheless, a significant proportion of individuals have continuing severe and persistent problems with social functioning, even after 12 months of specialist EIS provision⁸. Cases which show poor response to EIS often represent a subgroup who, although presenting with first episode psychosis, often have chronic severe and complex mental health and social functioning problems that date back pre-morbidly to childhood predating the onset of psychosis by many years⁸. The types of problems associated with social recovery in FEP are complex and include: poor engagement with service providers; loss of role and social contacts; perceived stigma and shame; anxiety and depression; and treatment resistant psychotic symptoms⁹. These persistent difficulties often result in lifelong patterns of social withdrawal¹⁰. Addressing these issues at an early stage is key as we have known for decades that the presence of persistent early social decline is associated with a poor long term course in schizophrenia¹¹. In addition to the personal consequences of functional disability, there are large financial implications for society, with much of the cost of psychosis resulting from lost productivity¹².

There is a need for new interventions targeting functional and social recovery in FEP. Whilst conventional Cognitive Behavioural Therapy (CBT) for psychosis has some evidence of effectiveness on social disability as a secondary outcome even where the primary focus has been on reducing positive symptoms of psychosis¹³. More specific adaptations of CBT for psychosis targeting negative symptoms and social recovery have shown promise¹⁴⁻¹⁶. Functional interventions such as Individual Placement and Support (IPS) have been found to be effective in helping individuals to return to paid employment¹⁷. However, IPS is most successful with individuals who are motivated to engage and wish to work and may be less effective for individuals who have poor engagement, who are ambivalent about change, and

who continue to experience comorbid difficulties¹⁷. Intervention needs to target a wider construct of social recovery than work alone. This includes education and voluntary work, as well as household activity and childcare, which are productive economic activities. Pro-social activity with peers is also key in ensuring young people achieve development milestones and continue to thrive at a key stage in life. Such principles are consistent with the user oriented goals identified by the recovery movement^{18,19}.

We have developed an intervention which focuses on social recovery. The rationale behind Social Recovery Therapy (SRT)⁹ is that 'in vivo' multi-systemic assertive outreach and case management are necessary to encourage more socially withdrawn individuals back into social environments, whilst the techniques of CBT are necessary to promote engagement and overcome the symptoms that impede this. It is the intensive and novel combination of these elements of therapy that provides the possibility of making meaningful changes to the lives of very withdrawn and difficult to engage young people who have not previously responded to standard EIS provision.

Preliminary evidence for the efficacy of SRT derives from the ISREP MRC trial platform study which suggested that the intervention can improve social recovery in individuals in the early stages of psychosis and is cost-effective^{14,20}. In the ISREP trial, unemployed adults with up to 8 year histories of non-affective psychosis showed significant improvements in structured activity, symptoms, hopelessness and rates of employment after receiving 9 months of SRT. Whilst the findings of the ISREP study are promising, targeting social disability at an even earlier stage may improve outcomes.

The objective of the present study is to evaluate the efficacy of adding SRT to EIS with the aim of achieving a step-change in early social recovery in young people who have severe and persistent social disability despite receiving EIS services for over a year after their first episode of psychosis. The primary hypothesis was that augmenting EIS with SRT would lead to improvements in time spent in structured activity at 9 months. The secondary hypotheses were that the effects on activity would persist at 15 months and that there would be benefits on general psychopathology and negative symptoms.

METHODS

Study Design

The study was a single blind, phase 2 trial, comparing the augmentation of EIS with SRT with provision of EIS alone. The study was conducted in 4 well established Early Intervention Services in the UK. The intervention lasted for 9 months with assessments at baseline, end of therapy (9 months); and 15 months (6 months after the end of therapy). The primary outcome was hours per week engaged in structured activity post-intervention at 9 months, assessed using the Time Use Survey. Ethical approval for the study was granted by the National Research Ethics Service (NRES) Committee, in the Black Country, West Midlands (Ref: 12/WM/0097).

Participants

Study inclusion criteria were: (1) patients with non-affective psychosis; (2) clients of EIS in Birmingham, Lancashire, Norfolk and Sussex (in the UK criteria for entry into EIS is operationally defined as having psychotic symptoms at or above PANSS 4); (3) showing a low level of structured activity after at least one year of treatment from EIS (defined as 30 hours or less per week on the Time Use Survey); (4) clients had been with EIS between 1-2 years; and (5) both males and females aged between 16-35 years. Participants were excluded if they: (1) were part of the original National EDEN cohort (2); did not speak adequate English to engage in the intervention; and (3) were considered too unwell to engage with the intervention. Potential participants were approached by their care co-ordinator and asked if they were willing to discuss the trial with a research assistant (RA). Information about the trial was shared verbally and via the participant information sheet. Written informed consent for screening and full participation in the study was taken by the RA. Participants were made aware that they could withdraw at any time, without any consequences for their treatment.

Randomisation and masking

Participants were randomly assigned to SRT plus EIS or EIS alone in a 1:1 ratio using an automated, concealed, computer generated allocation sequence generated by Norwich Clinical Trials Unit independently of the trial team, and were stratified by gender and

recruitment centre (Norfolk, Birmingham, Lancashire, Sussex). The randomisation sequence used permuted blocks with randomly varying block size.

Email notification of the allocation was sent automatically to therapists and the trial manager. An email notification confirming that the participant had been randomly assigned (with no information about group allocation) was sent to the RA, thus keeping them masked to group assignment. Therapists were also required to consider potential breaches in masking; and participants were reminded by assessors not to disclose treatment allocation. When masking was broken, another rater who was masked to group assignment assessed the participant at all subsequent timepoints.

Interventions

Early Intervention Service (EIS)

All participants received EIS provision from specialist teams. The teams in Birmingham, Lancashire, Norfolk and Sussex are all recognised centres of excellence for delivery of EIS. They all demonstrate high fidelity to the EIS model, indicating services which had the availability to deliver a comprehensive range of interventions²¹. These interventions include intensive and assertive recovery oriented case management; supported employment; peer support; group interventions; family work and CBT for psychosis as well as psychiatric medications and medical and psychiatric monitoring. All participants had an EIS case manager who provided oversight of their care and remained in contact with the participant throughout the trial.

Social Recovery Therapy (SRT)

In the treatment condition, care from EIS was augmented by SRT delivered by a therapist who was trained and supervised by the trial team. All therapists were supervised and accredited CBT therapists with experience in the participating EIS services. SRT practice in this trial was designed and supervised to ensure it was carried out in partnership with the EIS care.

The specific therapeutic procedures used in SRT were developed by DF, PF and JH. They draw from our experience in the MRC ISREP trial platform¹⁴ and details are provided in our published manual⁹. In summary SRT is delivered in three stages as follows:

Stage 1: Engaging and developing a Formulation. This consists of establishing a working therapeutic relationship to facilitate engagement and identify a problem list. Alongside this is a detailed assessment of personal motivation and premorbid hopes, expectations and goals which may have changed or altered with respect to the impact of illness. Specific behavioural assessment is carried out in vivo to assess how symptoms impact on activity. Links are identified between personally meaningful values and goals and achievable day-to-day activity targets.

Stage 2: Preparing for new activities. The client and therapist work together to identify pathways to meaningful new activities. This includes referral to relevant vocational agencies, education providers, and community providers of social or sports activities. Cognitive work at this stage involves promoting a sense of agency and addressing hopelessness, feelings of stigma, and negative beliefs about self and others. Behavioural experiments start focussing on managing symptoms while engaging in activity.

Stage 3: Engaging in new activities. This involves the active promotion of social activity using behavioural experiments, and fostering feelings of mastery and agency. The behavioural experiments are progressively shaped to address specific problems presented by individuals. Therapists adopt an assertive outreach style of contact, most frequently visiting people at home, or in community settings. Therapists are also encouraged to work systemically with family members, employers and educational providers to discuss and overcome potential problems which may represent blockages to social recovery.

Therapy competence and fidelity to SRT model

All trial therapists had formal training in CBT. In addition, they received specialist training in the SRT approach via workshops and regular supervision sessions from the trial therapy team including DF, PF and JH. The revised Cognitive Therapy Rating Scale²² was used to ensure therapist competence. All therapists were required to score above 36 from tape rated sessions and an average of above 3 on each item. Adherence to the SRT model was also assessed using a specific checklist. This method used a combination of independent expert rating of case notes and therapist ratings of individual sessions to assess techniques applied in individual sessions. A sufficient dose of therapy was defined as at least 6 sessions,

including the presence of an assessment and formulation phase and active behavioural experiments occurring in at least two independent sessions.

Outcomes

Study assessments took place at baseline, 9 months (post-intervention), and 15 months (6 months post-intervention). RAs visited participants at home to undertake assessments and used flexible strategies to maintain engagement with participants such as re-arranging missed appointments to maintain participation. Inter-rater reliability on outcome measures was ensured via regular training sessions for RAs and fortnightly telephone supervision meetings to discuss assessment queries. Data were collected according to the original funded protocol as submitted to and approved by the National Research Ethics Service (NRES) Committee, in the Black Country, West Midlands (Ref: 12/WM/0097). A briefer protocol summarising only the primary and secondary outcomes was published as the registered trial protocol. We report all data collected in this paper.

The trial was conducted in accordance with Good Clinical Practice (GCP) and the data analysed according to a Statistical Analysis Plan (SAP) developed prior to the unblinding of data, dated 06/11/2015. The SAP differed from the original ISCTRN protocol in that it was more specific in identifying the analysis of primary outcome as time use at 9 months, and also identified a range of secondary outcomes. These changes to the analysis plan took place after the ISCTRN protocol was published in June 2012 following further methodological review and particularly taking into account considerations of multiplicity for the analysis of primary outcome, in particular avoiding type 1 error through multiplicity²³. These changes were discussed with and approved by the Trial Steering Committee and were recorded in the trial documentation.

Primary Outcome

The primary outcome measure was Structured Activity measured by the Time Use Survey (TUS) as adapted for work in this client group²⁴ assessed at 9 months. The TUS is a semi-structured interview which enquires about time spent over the last month in work, education, voluntary work, leisure, sports, housework/chores, and childcare. Time spent on

each of the activities is calculated in terms of the average number of hours per week. The activities are summed to create two scores: 'Constructive Economic Activity' (work, education, voluntary work, housework/chores, and childcare) and 'Structured Activity' (Constructive Economic Activity plus leisure and sports activities). The TUS has been adapted from a version developed by the UK Office for National Statistics²⁵ enabling activity levels to be directly compared with age-matched non-clinical peers. On average, a non-clinical group aged between 16-36 years engage in 63.49 hours of structured activity per week, and activity levels below 30 hours are indicative of poor social functioning²⁴. The intra-class correlation coefficient (ICC) for inter-rater reliability on the TUS was .99. The TUS was also administered at 15 months. Structured Activity and Constructive Economic Activity at 15 months were recorded to explore the tenacity of the treatment effect. However, the SAP is clear that the primary outcome for the study was the TUS at 9 months.

Secondary Outcomes

The Positive and Negative Syndrome Scale (PANSS)²⁶ was used to assess general psychopathology and negative symptoms as secondary outcomes. Other secondary outcomes at 9 and 15 months included the Schedule for the Assessment of Negative Symptoms (SANS)²⁷; the Social Interaction Anxiety Scale (SIAS)²⁸; the Beck Depression Inventory-II (BDI-II)²⁹; the Beck Hopelessness Scale (BHS)³⁰; the Meaning in Life Questionnaire (MLQ)³¹; and the Adult Trait Hope Scale (ATHS)³².

Health Economic Outcomes

The Client Service Receipt Inventory (CSRI)³³ and the EuroQol-5D³⁴ were administered in order to conduct a health economic evaluation of the intervention. These were included in the trial protocol as secondary outcomes but are not reported here as they are the subject of another paper.

Mediators

A range of other scales were included to assess potential mediation of outcome. The Quality of Life Scale (QLS)³⁵ and the Role and Social Global Functioning Scales (RSGF)³⁶ were included in the original trial protocol as secondary outcomes but are not reported here as are the subject of another paper investigating mediation effects. Other mediator variables

included the Schizotypal Symptoms Inventory (SSI)³⁷; the Brief Core Schema Scales (BCSS)³⁸; and a range of neuropsychological variables. Data from these variables are also the subject of another paper investigating mediation effects.

Safety and Adverse Events

Serious and adverse events were recorded over the course of the trial using standard operating procedures and reported to the NHS research ethics committee.

Statistical Analysis

Analysis of the primary outcome was by intention to treat. The planned recruitment to the trial was based on a sample size of 150 individuals. A consensus group of clinicians and service users had conservatively estimated the minimum clinically significant gain on the primary outcome as 4 hours on the Time Use Survey. With a standard deviation of 8 hours and a minimum clinically important difference of 4 hours, we had 90% power to detect a difference of 4 hours to be significant at the conventional alpha level (two sided) of 5% with 150 subjects randomised 1:1, recruited across 4 sites. The trial as designed had 80% power to find the same effect with 120 evaluable patients.

The primary outcome was assessed using generalised mixed models, with an identity link and Gaussian/mixed error. Each subject contributed two observations; one at baseline and one at 9 months. The model included indicators for whether the observation is baseline or 9 months, and whether or not the subject was randomised in that period to receive the active intervention or control. In addition, all models included the stratification variables as patient level explanatory factors (gender and recruitment centre). Observations were linked using random intercept terms within a patient. Denominator degrees of freedom were derived from the number of patients. Supportive analyses were conducted using the separate components of the primary outcome. In addition, the primary outcome was analysed using residual (r side) random effects instead of generalised (g side) random effects. A further supportive analysis was undertaken including baseline score as a patient level explanatory variable.

The principal analysis was planned on all available subjects by intention to treat, without imputation of missing values. Missing data were assumed to be *missing not at random*.

Supportive analyses addressed missing data patterns by modelling jointly the continuous outcome score (with Gaussian error) and observed loss to follow up (with Bernoulli error), to describe the joint probability of the observed outcome. The joint (multivariate) models require the assumption that those who provide missing data are, on average, poorer performers than those who did not drop out. This defensible assumption simply implies that loss to follow up is a measure of poor performance on the scale of interest. All analyses were conducted in SAS software, Version 9.4 (SAS Institute Inc, Carey NC, USA).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

RESULTS

Participants were recruited over 20 months between 1st October 2012 and 30th June 2014. A CONSORT diagram showing study design and participant flow through the study up to randomisation and treatment allocation is shown in Figure 1. The final sample size was 154 (39 Birmingham, 53 Lancashire, 47 Norfolk and 16 Sussex) with 75 randomised to EIS plus SRCBT and 79 randomised to EIS alone. The independent data monitoring and ethics committee monitored all serious and adverse events. The committee found no serious or adverse events attributable to the therapy.

Table 1 provides baseline demographic characteristics of the sample by treatment and control conditions. The sample were predominantly male, single and of White British/Irish/Other ethnicity. Length of illness and duration of untreated psychosis were variable but, as per the study inclusion criteria, all participants had been engaged with EIS for between 12 and 30 months. Table 2 provides means and medians of baseline, primary and secondary outcomes by treatment and control conditions and Table 3 provides results of the prespecified statistical analysis plan. Tables 4 and 5 provide data for mediator variables. Of note is the severity of social disability, psychotic symptomatology, anxiety and depression present in the sample at baseline.

Participants allocated to the EI plus SRCBT condition received a mean of 16.49 sessions of SRT (SD = 8.39; range 0 to 37). Competence in cognitive therapy as assessed by the CTS-R was excellent. Of the random selection of therapy tapes rated independently, 27/30 (90%) scored higher than the cut off based on the therapy protocol. Adherence ratings on the SRCBT checklist indicated that 61 (81.3%) participants received a sufficient dose of SRT. Seven participants dropped out and did not have ratings available, and 7 did not receive a sufficient dose.

As can be seen in Tables 2 and 3, for the primary outcome at 9 months, 143 participants (93%) provided data on the primary outcome (7% missing data overall, with 2.67% in the SRT plus EIS group and 11.39% in EIS alone). This was regarded as satisfactory for an intention to treat (ITT) analysis. The primary ITT analysis indicated that the intervention (SRT plus EIS) was associated with a large and clinically important increase in structured activity 8.1 hours (95% CI 2.5 to 13.7; $p = 0.0050$) compared with EIS alone at 9 months. The supportive analysis using a repeated measure analysis (residual random effect) provided a similar estimate (8.8 hours; 95% CI 1.3 to 16.3). The supportive analysis utilising baseline value as a patient level explanatory variable provided an estimate of 8.9 hours (95% CI 1.4 to 16.5).

For secondary outcomes, despite considerable effort to retain participants, the missing data were greater, particularly for face-to-face assessments. For time use at 15 months there were 17% missing data overall (9% for SRT plus EIS and 24% for EIS alone). For the PANSS missing data were 20% total (12 % SRT vs 28% EIS) at 9 months and 35% total (24% SRT vs 41% EIS) at 15 months. The pattern of missing data was clearly biased, with greater missing data in the EIS alone condition, and was thus regarded as Missing Not at Random.

A completer case analysis was first used for the analysis of secondary outcomes, in accordance with the protocol and the Statistical Analysis Plan. In addition, a joint modelling (multivariate) strategy was applied to account for missing data. This approach assumes that loss to follow up is associated with poor performance on the scale of interest. The analysis of secondary outcomes by both completer analysis and the results of the joint models, which provide p values alone, are described in Table 3.

Analysis of treatment effects for Time Use at 15 months and other secondary outcomes using completer analysis showed no systematic differences between experimental conditions. However the results of the joint models provided supportive evidence that, conditional on the assumption that loss to follow up is associated with a poorer score on time use, the observed results are consistent with systematic differences in several secondary outcomes. These include: structured ($p=0.037$) and constructive economic ($p=0.046$) time use at 15 months; PANSS negative symptoms ($p=0.032$) and general psychopathology ($p=0.043$) at 9 months; SIAS at 9 months ($p=0.016$); BHS at 9 months ($p=0.020$) and 15 months ($p=0.022$); Trait Hope at 15 months ($p=0.0060$); and MLQ at 15 months ($p=0.043$).

DISCUSSION

The primary aim of this study was to establish the presence of a treatment effect in a subgroup of patients we know to be hard to treat, who tend not to engage and have complex problems, and are the poorest outcome EI subgroup for whom there is no existing effective treatment. The study was powered on an effect on the primary outcome at 9 months. The result at 9 months for the primary outcome is clear and definitive. The participants who received SRT plus EIS achieved an improvement of greater than 8 hours per week in their level of structured activity compared to those receiving EIS alone. Hence, those receiving SRT in combination with EIS provision made a large, significant and clinically important gain in activity compared to those receiving EIS alone after 9 months of intervention. This is the first study to demonstrate a significant improvement in functioning in this already highly disabled group. The size of the effect is twice that which consensus groups of users and clinicians had identified as the minimum clinically important difference, and it represents an amount of activity equivalent to a working day. The evidence from the primary analysis is therefore clear that SRT may have a clinically important effect in promoting earlier social recovery in comparison to EIS provision alone.

The key issue for secondary outcomes was whether or not this effect persists at 15 months. The main problem was a high rate of missing data at that point. This meant all analyses of secondary outcomes lacked power and were difficult to interpret. This population is incredibly challenging to keep in follow up and the excellent response rate for the primary outcome is a tribute to the efforts of the field researchers involved in the study.

Missingness is clearly related to the outcomes of interest as availability for assessments by participants is related to social engagement, and social recovery therapy specifically aims to increase social engagement. At all assessment points many more participants were available for follow up assessments in the SRT group than in the EIS alone group. Loss to follow up at 15 months for TUS is over twice the rate in the control condition as in the experimental group (9.3% vs 24.1%). This in itself may imply an effect of the intervention on engagement which most clinicians would regard as useful and worthy of examination in a future study. However, the pattern of differential missingness represents a challenge to interpreting the effect at 15 months as it may formally be regarded as *Missing not at random*. Completor analysis suggests that the means the outcomes at 15 months are similar between the groups but this may be biased if it is the worst outcome cases who dropped out. The joint models analysed simultaneously the outcome of interest and the binomial of missing values for that outcome and was intended to provide a least biased assessment appropriate to the data being *Missing not at random*. Modelling the two values simultaneously in the multivariate model accounts for bias and provides a more encouraging overall p value for the difference between the two experimental conditions $p = 0.037$. Although reliant on the assumption that drop out equals worse outcome on the scale of interest, the joint modelling analyses provide encouragement that at least some of the effect of the experimental treatment on time use may remain at 15 months, albeit with a level of attenuation when compared with the similarly derived 9 month values. A limitation of the joint modelling approach is it provides only a p value for the combined pseudolikelihoods of the outcome and drop out, and cannot provide an updated estimate or confidence interval for the treatment effect.

A further question for secondary outcomes was the effect on negative symptoms and general psychopathology as assessed by PANSS. Again the presence of large degree of missing data does not allow a firm conclusion about these outcomes and the completor analysis suggests there is no effect, but the joint modelling which attempts to account for missing data suggests an impact on these outcomes at 9 months.

Of the 206 individuals identified as meeting inclusion criteria, a large proportion (75%) consented and were randomised into the study. This was the result of intensive and assertive recruitment procedures. The RAs worked in an assertive outreach manner, visiting

participants at home and engaging them into the study. The result was the recruitment of a group with very severe and stable social disability. The total time spent in activity by the group recruited for the study was less than 12 hours per week, compared to over 60 hours per week in an age-matched non-clinical sample²⁴. This was a group of young people with extreme social withdrawal who also had a wide range of other comorbid and complex comorbidities, including high levels of treatment resistant and residual positive psychotic symptoms, negative symptoms, anxiety and depression, as well as the presence of current hopelessness and a lack of hope for the future.

The present study extends the previous ISREP trial platform study of SRT which compared SRT to treatment as usual in finding a benefit at 9 months and at 15 months and 2 year follow up, and with associated gains in secondary outcomes and cost effectiveness^{14,20}. The present study represents a more rigorous test as in this study the comparator intervention was a highly active treatment, EIS provision. Treatment as usual in the present study consisted of high quality EIS provision in sites with good fidelity to the EIS model, as recommended by NICE guidelines for psychosis and schizophrenia³⁹. Improvements were observed in both treatment conditions but with differential improvement in the SRT arm.

A strength of this study was good internal and external validity for the trial on the primary outcome. The study was conducted with a high degree of rigour with all researchers and therapists involved in the study receiving regular supervision and with routine checks on inter-rater reliability and adherence to the therapy model.

A limitation of the study was that it was compromised by the level and pattern of missing data in the secondary outcomes, albeit one that was addressed using joint modelling. The characteristics of the target group in this study being by definition a difficult to engage and extremely withdrawn sample represent a challenge to researchers, especially where follow up assessments are reliant on face to face assessments. Potentially future studies in this area might maximise rate of follow up by focussing on hard proxy variables of engagement in services which may be derived from records rather than face to face assessments especially as engagement is of itself an important outcome in this population. A further limitation of this study was that many of the secondary outcomes have wide confidence intervals (an indication of low statistical power) suggesting low precision or uncertainty in

the estimation of treatment effects. Further the study was by necessity single blind, and thus may be affected by the experience of the subject in receiving therapy.

The target group for this study was a particularly severe group of young people with first episode psychosis who we know are likely to have poor long term outcomes. This study provides encouragement for EIS practitioners to focus on this subgroup who are often neglected and adopt these type of practices. This is the first study to show benefits for this group. The effect size after treatment is clearly of clinical benefit, especially given the extreme social withdrawal present at baseline. Furthermore, the very fact of differential drop out with many more receiving treatment being available to follow up than in the control implies benefits on maintaining engagement in the treatment group which may be important to assess as an outcome in and of itself in future work. The degree to which the treatment results in persistence of gains and longer term effects deserves further study. Joint modelling aimed to account for the bias associated with the differential pattern of missingness in the analysis and suggests the potential for persistence of effects over the longer term, but as this was a supplementary analysis, persistence of gains cannot be established. A larger more definitive trial is required to examine more clearly effects over the longer term. The extent to which interventions of this type may be enhanced by 'top up' therapy or greater numbers of sessions over a longer duration may be worthy of further scrutiny given evidence from similar studies in adults with more established schizophrenia¹⁶.

Competing Interests

All authors declare that they have no competing interests.

Author Contributions

DF was CI for the trial and wrote the first draft of the manuscript with JH. NF analysed the data. JH, PF, MM, NF, PM, LE, AL, PJ, TA, SS, VS and MB are key investigators on the SUPEREDEN programme of work and contributed to the study design. All authors contributed to and have approved the final manuscript.

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Figure 1. Trial Profile

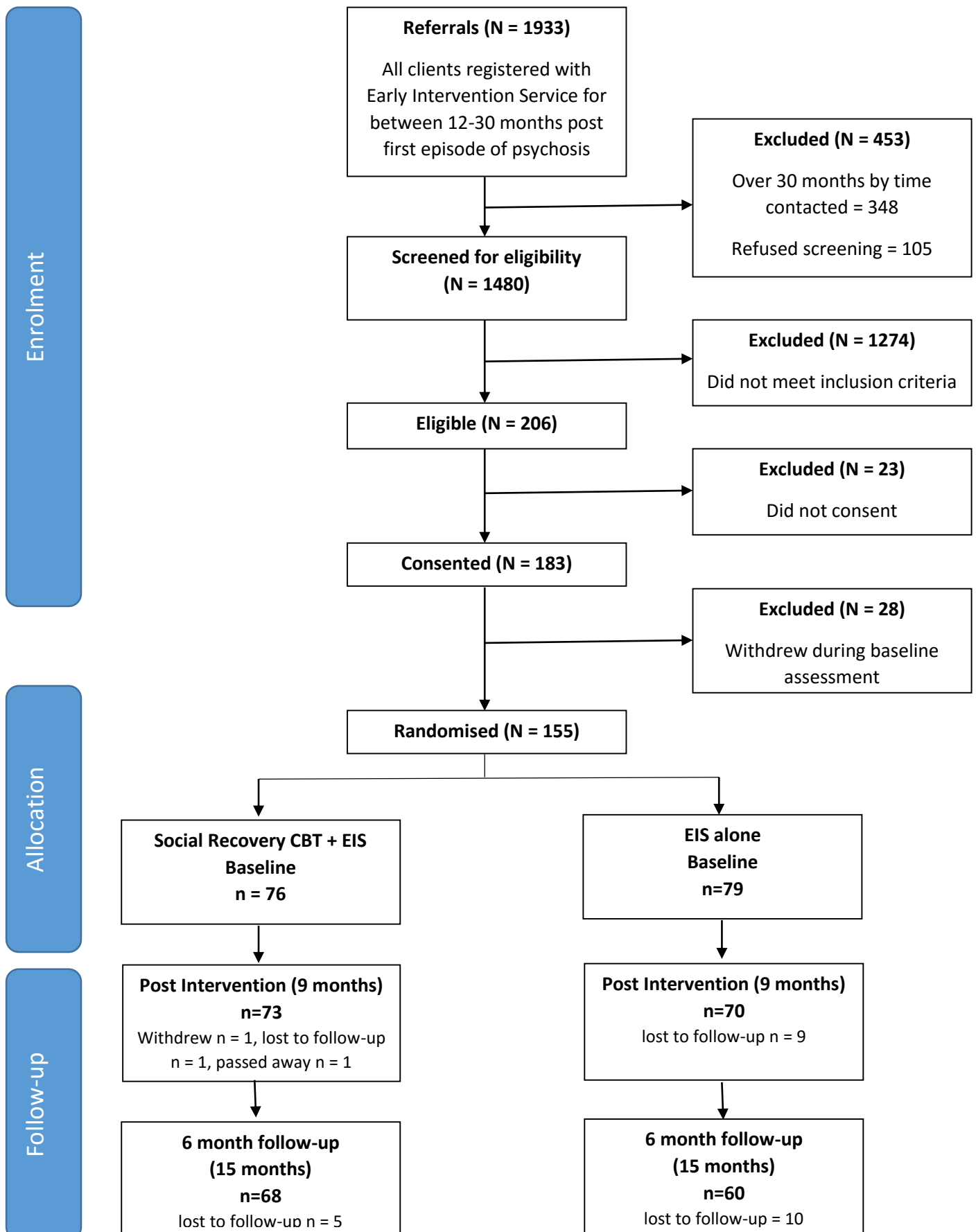


Table 1

Baseline Demographic Information for the Intent to Treat Population

Item	Standard Care n=79	SRCBT + Standard Care n=75
Male n (%)	60 (75.95%)	56 (74.67%)
Age, median (IQR)	24.15 (22.17, 27.79)	24.84 (20.73, 29.04)
Length of illness in months, median (IQR)	26 (20, 38)	23.5 (17, 33)
Duration of Untreated Psychosis in days, median (IQR)	66 (20, 240.75)	73 (13, 316)
Premorbid Adjustment, mean (SD)		
Early Adolescence	0.34 (0.15)	0.33 (0.20)
Late Adolescence	0.36 (0.17)	0.34 (0.17)
Years in Schooling	12 (11, 12)	12 (11, 13)
Ethnic Group		
British	58 (73.42%)	55 (73.33%)
Irish	2 (2.53%)	1 (1.33%)
Any other White background	1 (1.27%)	2 (2.67%)
White and Black Caribbean	2 (2.53%)	0 (0%)
White and Black African	0 (0%)	1 (1.33%)
White and Asian	0 (0%)	2 (2.67%)
Any other mixed background	0 (0%)	1 (1.33%)
Indian	1 (1.27%)	0 (0%)
Pakistani	6 (7.59%)	7 (9.33%)
Bangladeshi	1 (1.27%)	1 (1.33%)
Any other Asian background	1 (1.27%)	1 (1.33%)
Caribbean	4 (5.06%)	0 (0%)
African	2 (2.53%)	1 (1.33%)
Any other Black background	0 (0%)	1 (1.33%)
Any other ethnic group	1 (1.27%)	2 (2.67%)
Mother Tongue		
English language	75 (94.94%)	69 (92.0%)
Other language (but having good knowledge of English language)	4 (5.06%)	6 (8.0%)
Marital Status		
Single	69 (87.34%)	67 (89.33%)
Cohabiting	5 (6.33%)	4 (5.33%)
Married	3 (3.80%)	4 (5.33%)
Divorced	2 (2.53%)	0 (0%)

Table 2

Primary and secondary outcomes at baseline, 9 months and 15 months

	Baseline		9 months		15 months	
	SRT +EIS	EIS alone	SRT +EIS	EIS alone	SRT + EIS	EIS alone
Primary Outcomes						
Structured activity	11(7.5) n=75	12(8.6) n=79	26.6(24.2) n=73	18(20) n=70	23(19) n=68	22.5(23.3) n=60
Constructive economic activity	7.5(6.1) n=75	7.9(7.5) n=79	20.1(22) n=73	14.1(20) n=70	16.4(17) n=68	16.5(23.3) n=60
Secondary Outcomes						
PANSS*	62(27) n=75	65(27) n=79	54(34) n=66	58(18) n=57	48(28) n=57	56(25) n=46
SANS*	23(21) n=74	27(18) n=78	19(22) n=64	18(23) n=57	20(26) n=57	21(21) n=47
BDI*	18(19) n=73	19(21) n=75	12(21) n=62	16(16) n=55	9(18) n=55	8(16) n=43
SIAS*	40(20)	40(22)	37(28)	37(20)	36(27)	34(30)

	n=69	n=72	n=64	n=53	n=56	n=43
BHS*	8(8) n=67	9(7) n=67	5(7) n=59	7(9) n=56	4(6) n=56	5(8) n= 42
ATHS Sense of agency*	15(10) n=68	18(11) n=67	19(11) n=54	17(12) n=46	21(7) n=53	19(10) n=40
ATHS Optimism*	20(8) n=68	19(11) n=67	21(7) n=54	20(8) n=46	22(7) n=53	20(6) n=40
Meaning in life*	39(11) n=67	42(14) n=68	40(13) n=56	42(12) n=46	40(12) n=52	41(18) n= 40

Note. Data are mean and SD unless indicated by * in which case median and interquartile ranges. Some scales have missing data and numbers are provided to indicate sample without complete data. PANSS= Positive and Negative Symptom Scales; SANS=Scale for Assessment of Negative Symptom; BDI= Beck Depression Inventory; SIAS- Social Interaction an Anxiety Scales; BHS=Beck Hopelessness Scales; ATHS= Adult Trait Hope Scale; MLQ= Meaning in Life Questionnaire

Table 3

Results of prespecified outcome analysis and joint models for primary and secondary outcomes

Analysis	Estimate	Lower 95% CI	Upper 95% CI	P	Missing (intervention) N = 75 r(%)	Missing (Control) n = 79 (r(%))	P value Joint Model
Primary Outcomes							
Structured Activity at 9 months	8.080	2.502	13.657	0.0050	2 (2.7%)	9 (11.4%)	0.011
Constructive Economic Activity at 9 months	5.859	0.790	10.928	0.024	2 (2.7%)	9 (11.4%)	0.034
Secondary Outcomes							
Structured Activity at 15 months	0.054	-5.154	5.262	0.98	7 (9.3%)	19 (24.1%)	0.037
Constructive Economic Activity at 15 months	-0.506	-5.048	4.036	0.83	7 (9.3%)	19 (24.1%)	0.046
Positive PANSS 9 months	0.306	-1.228	1.840	0.69	9 (12.0%)	22 (27.9%)	0.068
Negative PANSS 9 months	-1.020	-2.662	0.622	0.22	9 (12.0%)	22 (27.9%)	0.032
General PANSS 9 months	-1.014	-3.514	1.486	0.42	9 (12.0%)	22 (27.9%)	0.043
Positive PANSS 15 months	1.219	-0.632	3.071	0.19	18 (24.0%)	32 (40.5%)	0.071
Negative PANSS 15 months	-0.629	-2.411	1.152	0.49	18 (24.0%)	32 (40.5%)	0.073
General PANSS 15 months	-0.084	-3.031	2.862	0.96	18 (24.0%)	33 (41.8%)	0.081
SANS Total at 9 months	9.713	-14.568	33.994	0.43	11 (14.7%)	20 (25.3%)	0.17
SANS Total at 15 months	16.798	-10.553	44.147	0.23	18 (24.0%)	32 (40.5%)	0.035
BDI at 9 months	-1.567	-4.840	1.706	0.35	13 (17.3%)	24 (30.4%)	0.10
BDI at 15 months	0.748	-3.261	4.757	0.71	20 (26.7%)	36 (45.6%)	0.067
SIAS at 9 months	-2.559	-6.964	1.846	0.25	11 (14.7%)	26 (32.9%)	0.016
SIAS at 15 months	1.490	-4.132	7.111	0.60	19 (25.3%)	36 (45.6%)	0.10
BHS at 9 months	-1.464	-3.282	0.354	0.11	16 (21.3%)	33 (41.8%)	0.020
BHS at 15 months	-1.451	-3.257	0.355	0.11	19 (25.3%)	37 (46.8%)	0.022
ATHS total score 9 months	2.214	-1.504	5.931	0.24	21 (28.0%)	33 (41.8%)	0.15
ATHS total score 15 months	3.860	-0.266	7.987	0.066	22 (29.3%)	39 (49.4%)	0.0060

MLQ total score 9 months	2.193	-1.496	5.883	0.24	19 (25.3%)	33 (41.8%)	0.12
MLQ total score 15 months	0.782	-3.196	4.759	0.70	23 (30.7%)	39 (49.4%)	0.043

Note. PANSS= Positive and Negative Symptom Scales; SANS=Scale for Assessment of Negative Symptom; BDI= Beck Depression Inventory; SIAS- Social Interaction an Anxiety Scales; BHS=Beck Hopelessness Scales; AHS= Adult Trait Hope Scale; MLQ= Meaning in Life Questionnaire